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**REMARKS**

The present application was originally filed with 19 Claims. In a Restriction Requirement mailed July 1, 2003, the Examiner restricted the Claims into four Groups, with Claims 1-12, drawn to a method of producing a transformed microorganism in Group I; Claim 13, drawn to a library of mutants in Group II; Claims 14-17, drawn to directed evolution of a host cell chromosome in Group III; and Claims 18 and 19, drawn to a method for constructing a sequence of interest in Group 4. In a Response filed August 22, 2003, Applicants elected the Claims in Group I (Claims 1-12), and the species *Bacillus*, with the request that the remaining species be examined, upon the determination that the species *Bacillus* is patentable. Applicants have cancelled Claims 13-19, as well as Claims 2, 3, 8, and 9, without prejudice and reserve the right to pursue these Claims and/or similar Claims in one or more Divisional or other applications. Applicants appreciate the Examiner's withdrawal of many of the rejections presented in the previous Office Actions. The Examiner's maintained rejections are addressed in the following order:

- 1) Claims 1, 4-7, and 9-12 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being Indefinite;
- 2) Claims 1, 4-7, and 9-12 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly not meeting the written description requirement; and
- 3) Claims 1, 4-7, and 9-12 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not meeting the enablement requirement.

**1) The Claims are Definite**

The Examiner has maintained the rejection of Claims 1, 4-7, and 9-12, under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Examiner indicates that Applicants do not specify the reason for their traversal in the Response to Final Office Action filed August 20, 2004. Applicants must respectfully disagree and reiterate the arguments previously presented.

As indicated in the Response to Final Office Action, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 1 to recite non-homologous sequences (i.e., rather than "non-heterologous" sequences), cancelled Claim 9, and amended Claim 12.

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Applicants reserve the right to pursue the originally filed, as well as the amended, similar, broader, and/or narrower Claims in one or more subsequently filed applications.

The Examiner argues that "[t]he specification does not provide representative examples of DNA constructs to convey possession of the claimed invention. The specification does not provide examples of incoming sequences of a variety of lengths, for example. The specification does not provide examples of varying degrees of homology for the homology boxes, or variations in the size of homology boxes . . . ." (Office Action, page 4).

Applicants must respectfully disagree and submit that the Claims are definite, as the disclosure contained within the present Specification as filed, conveys to those of skill in the art that Applicants were in possession of the claimed invention at the time the application was filed. For example, the Figures provide teaching of the presently claimed invention, including varying homology box lengths, modifications of genes of interest, etc. The Examples likewise provide descriptions of various embodiments of the presently claimed invention. Applicants respectfully submit that the amended Claims are definite. Thus, Applicants respectfully request that this rejection be withdrawn.

## 2) The Claims Meet the Written Description Requirement

The Examiner has also maintained the rejection of Claims 1, 4-7, and 9-12 under 35 U.S.C. §112, second paragraph, as allegedly not meeting the written description requirement. In regard to Claim 1, the Examiner argues that "[i]t is not disclosed by the specification that non-heterologous sequences can function as non-critical targets for BacIII to initiate uptake of the DNA constructs of the claimed invention (but see, e.g., the instant Specification at p. 12, lines 13-27)." (Office Action, page 5). In order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 1 to recite non-homologous, rather than non-heterologous sequences.

With regard to Claim 9, the Examiner argues that "[t]he Specification as filed does not disclose stuffer sequences that flank non-homologous sequences that flank said homology boxes, as in claim 9, but instead state at p. 8, lines 5-9, that stuffer sequences means any extra DNA that flanks the homology boxes, typically vector sequences, but could be any non-homologous DNA sequence. Thus amended claim 9 may be interpreted to encompass stuffer boxes that flank stuffer boxes that flank homology boxes; there is no literal support, in the Specification as filed, for such a limitation." (Office Action, pages 5-6). While Applicants respectfully submit that Claim 9 is supported by the Specification as filed, in order to further the

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prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have cancelled Claim 9. Applicants reserve the right to pursue Claim 9, as well as similar, broader, and/or narrower Claims in one or more subsequently filed applications. As Claim 9 has been cancelled, the Examiner's rejection of this Claim is moot.

With regard to Claim 12, the Examiner argues that "[t]he Specification does not disclose how to increase the homology of a homology box." (Office Action, page 6). Applicants must respectfully disagree, as pages 3-4 of the Specification as filed describes this embodiment. Nonetheless, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 12 to recite the selection of a target sequence in a chromosome of the competent cell and increasing the homology between the target sequence and the construct. Applicants reserve the right to pursue Claim 12, as well as similar, broader, and/or narrower Claims in one or more subsequently filed applications. Applicants respectfully submit that Claim 12 meets the written description requirement and request that this entire rejection be withdrawn.

In the Advisory Action, the Examiner indicates that "... The Specification does not provide representative examples of different sizes or of non-homologous or non-heterologous DNA flanking sequences or varying degrees of homology or non-homology to convey possession of the claimed invention" (Advisory Action, page 2). Yet, in the same paragraph, the Examiner admits that "Figure 11 discloses non-homologous flanking regions of ~2 kb and ~1.5 kb." (Advisory Action, page 2). Thus, Applicants respectfully submit that the Specification as filed does indeed provide differing lengths of non-homologous flanking regions. Applicants respectfully submit that the combination of this Figure, taken together with the Specification as a whole does indeed show that Applicants were in possession of the claimed invention. Thus, Applicants respectfully request that this rejection be withdrawn.

### 3) The Claims are Enabled

The Examiner has also maintained the rejection of Claims 1, 4-7, and 9-12 under 35 U.S.C. §112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner indicates that Applicants do not specify the reason for their traversal in the Response to Final Office Action filed August 20, 2004. Applicants must respectfully disagree and reiterate the arguments previously presented.

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As indicated above, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, Applicants have amended Claim 1, cancelled Claim 9, and amended Claim 12. Applicants respectfully submit that these amendments and cancellations have overcome the Examiner's non-enablement rejection. Thus, Applicants respectfully submit that the amended Claims meet the enablement requirement and request that this rejection be withdrawn.

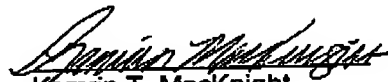
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**CONCLUSION**

All grounds of rejection and objection of the Final Office Action of July 27, 2004, having been addressed, reconsideration of the application is respectfully requested. Applicants respectfully submit that the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-5838.

Respectfully submitted,

Date: October 15, 2004

  
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